Data Analysis Projects
MoBi 4. FS - SS2019

Carl Herrmann

Health Data Science Unit - Medizinische Fakultät Heidelberg

Concept

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- **Project-oriented teaching**: provide hands-on experience with data analysis and programming

- **Goals**
  - experience data analysis challenges on real datasets related to research question
  - experience team work, also outside of your team!
  - learn to use modern data analysis tools: R / Python / markdown / notebooks / github

Research topics / projects

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- **5 research projects** have been defined
- Each topic has up to **5 sub-projects**
- Each project will be worked out by **groups of 4 students**
- **one supervisor and master tutor per project**
- **Role of the master tutors:**
  - weekly meetings with groups working on project (Wednesday 10am-1pm)
- Meeting rooms: BioQuant SR42/43 + IPMB meeting room 5th floor
  2 other meeting places must be found (lounge corner at BioQuant?…)
- Tutors:
  Valentina Giunchiglia; Julia Rühle; David Schwarzenbacher; Nicolas Peschke; Alexander Mattausch

Timeline

	We do…	*You do…*
17/04	Presentation of the projects	
24/04	Presentation of R markdown and github	selection of projects and teams; registration
15/05		Presentation of project proposal (10 + 10 min)
24/07 (25/07 for Project 03)		Final presentation (15+10 minutes)

Project proposal (15/05)

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- During the project proposal presentation, you should
  - review some of the references given in the project description
  - explain what the questions / challenges are
  - describe which of these questions you want to adress in your project
  - indicate a approximate timeline
    - milestones = important steps in the analysis
    - when these milestones should be achieved

- Presentation in front of the project supervisors
  - 10 minutes presentation
  - 10 minutes discussion / questions

- *All team members are expected to contribute!*

Projects / sub-projects

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- **Project 01**: ***Genetic interactions in cancer***

  (Ashwini Sharma / Carl Herrmann)

  - Data types: gene expression / gene mutations / gene knockdown / CNV

- **Project 02**: ***Cellular response to drug perturbation***

  (Nicolas Palacio / Javier Perales)

  - Data types: gene expression treated / untreated / mutations / metadata

- **Project 03**: ***Biomedical image analysis***

  (Karl Rohr / Christian Ritter)

  - Data types: MNIST images / cell nuclei images

- **Project 04**: ***Programming k-means***

  (Thorsten Beier)

  - Data types: scRNA-seq

- **Project 05**: ***Cancer DNA Methylation***

  (Matthias Schlesner / Christian Heyer)

  - Data types: DNA methylation WGBS

Project selection / registration

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- Listen to the description of the projects / sub-projects
- Check this webpage
  https://datascience-mobi.github.io/
- Once you have selected your team and project, **register your team** in the Google sheet
  https://docs.google.com/spreadsheets/d/1LEQLH2LaDulMq3Qepx-7-5KWjgZjK4dfWDDIbm1vu0Q/edit?usp=sharing

- ***Selection of the projects should be done by 24/04 10am !***

Organizing your work

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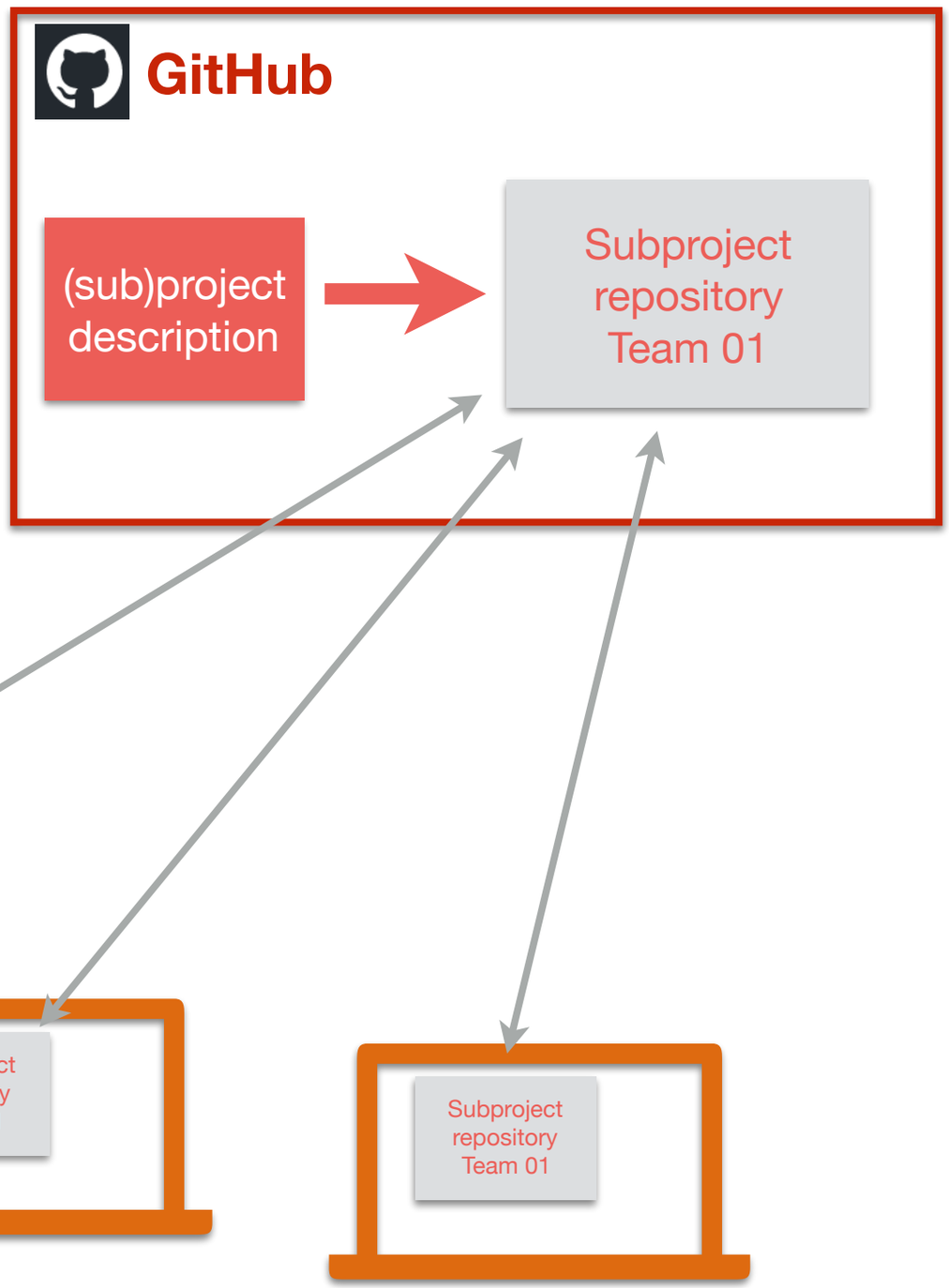
Website
datascience-mobi.github.io



jupyter

R Markdown
from RStudio

Project 01: genetic interactions in Cancer cells

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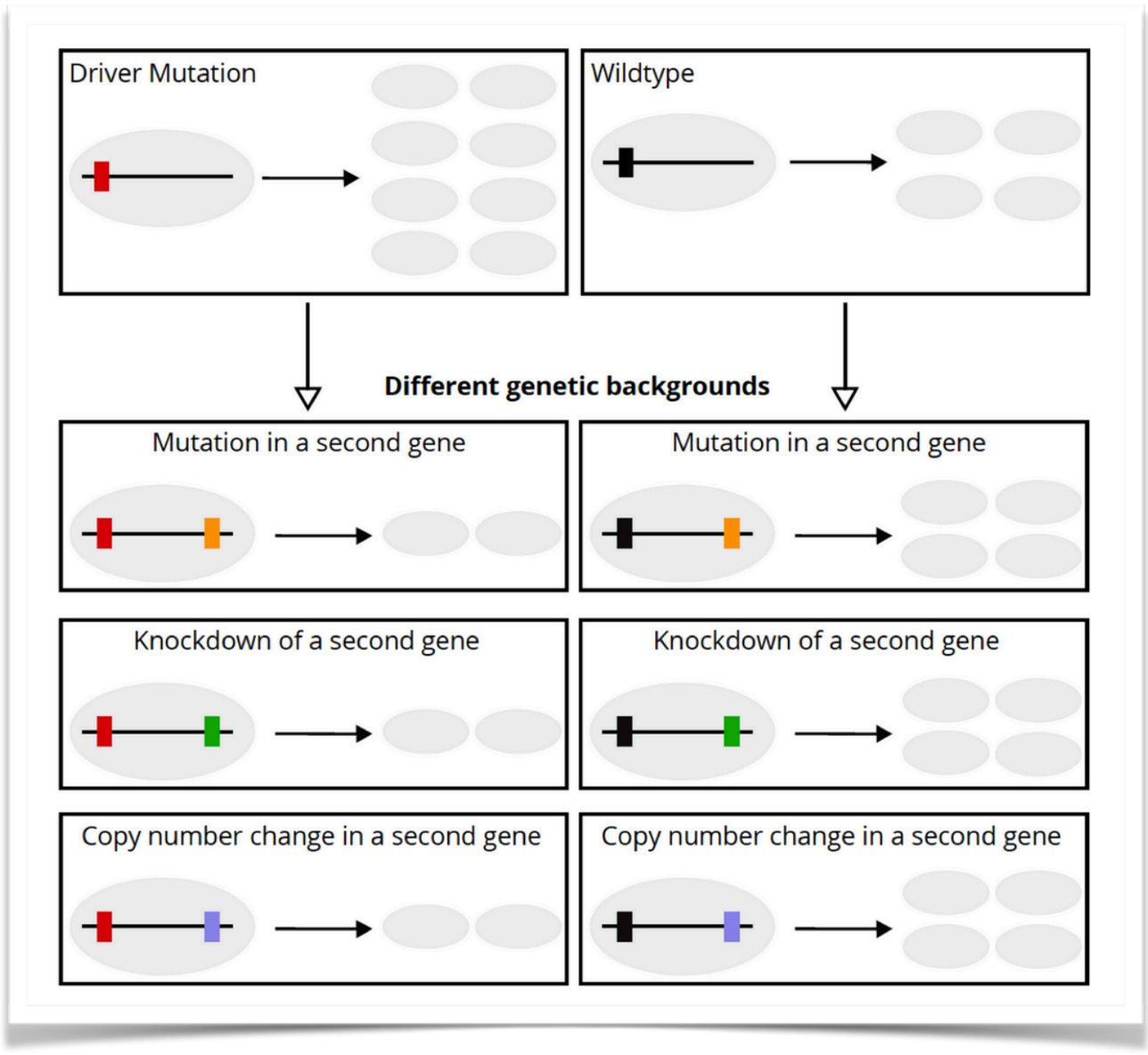
- Find **synthetic lethal interactions** in cancer cell lines for driver mutations
- Which mutation / copy-number alteration does lead together with a driver mutation to a significant phenotype in cancer cells?
  → identify potential therapeutic targets



Project 01: genetic interactions in Cancer cells

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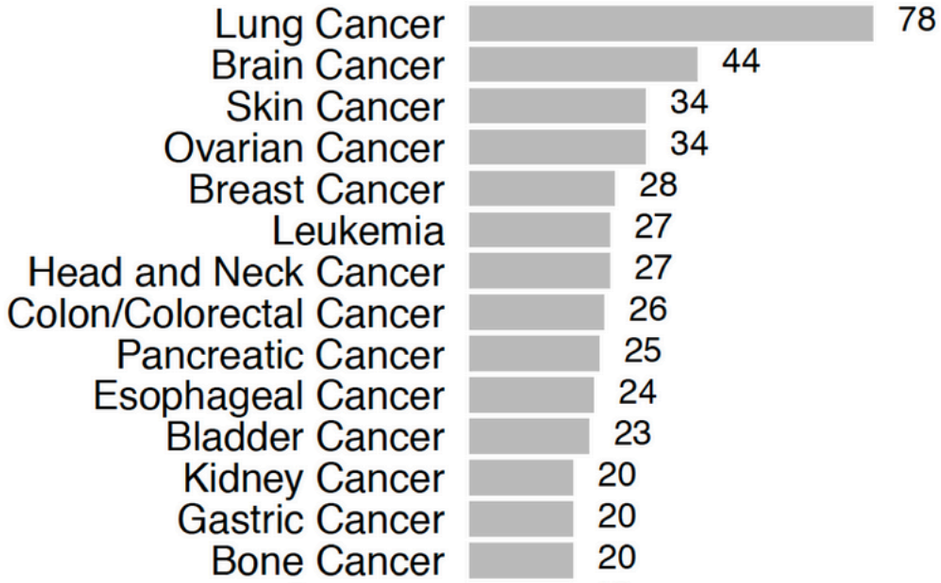
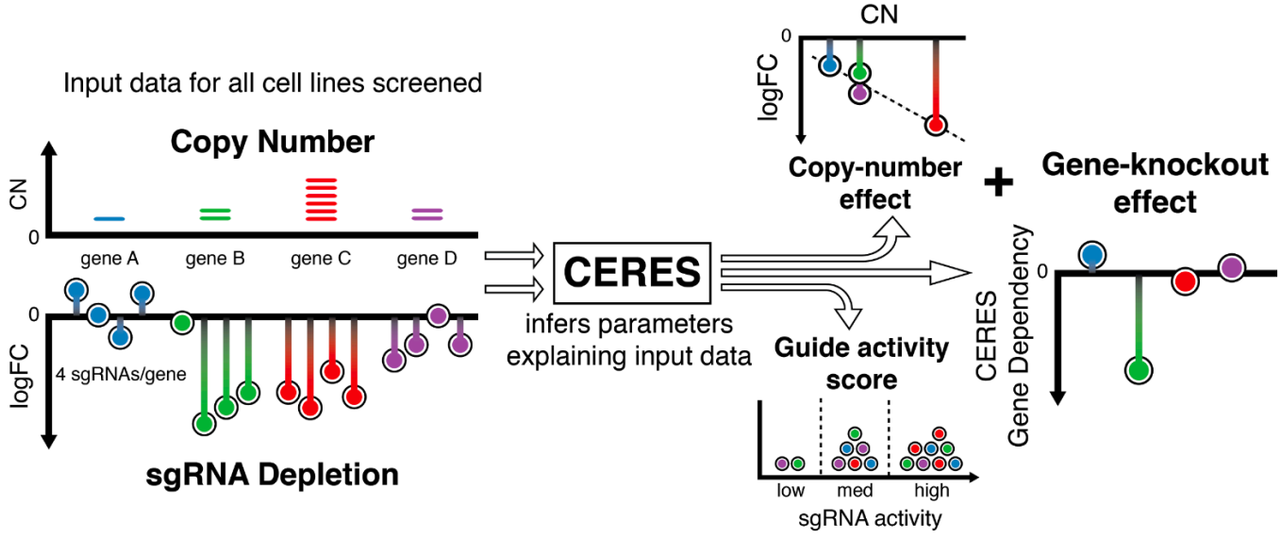
- Knockdown assays (Project DepMap/CERES): CRISPR-Cas9 for ~17.000 genes across 544 cell lines





[Meyer etal., 2017]

Datasets

- **Gene expression** in various cancer cell lines

	ACH-000004	ACH-000005	ACH-000007	ACH-000009	ACH-000011	ACH-000012	ACH-000013
TSPAN6	2.61588707	3.06695024	4.06608919	6.50795317	4.57773093	5.82094479	5.53387478
TNMD	0.00000000	0.00000000	0.00000000	0.09761080	0.00000000	0.00000000	0.05658353
DPM1	5.32337007	5.76261458	5.88996020	7.98162436	5.53574194	6.00652245	7.53216108
SCYL3	2.40599236	2.99276843	3.04963077	2.24792751	2.08746284	1.91456452	1.91073266
C1orf112	3.90207358	5.35966172	3.76022095	4.49121176	2.64616266	3.75167795	3.54720302
FGR	0.92599942	0.23878686	0.02856915	0.00000000	0.00000000	0.02856915	0.02856915
CFH	4.88898672	5.70016225	0.01435529	0.02856915	0.35614381	2.68929916	1.98550043

- **Mutations** in genes in each cell line & copy-number alterations in each cell line

Hugo_Symbol	Entrez_Gene_Id	NCBI_Build	Chromosome	Start_position	End_position	Strand	Variant_Classification
RNF207	388591	37	1	6279339	6279339	+	Missense_Mutation
PLEKHG5	57449	37	1	6533165	6533165	+	Missense_Mutation
PDPN	10630	37	1	13940848	13940848	+	Missense_Mutation
CASP9	842	37	1	15819484	15819484	+	Missense_Mutation
RAP1GAP	5909	37	1	21924552	21924552	+	Missense_Mutation
C1QC	714	37	1	22974054	22974054	+	Silent
CNKSR1	10256	37	1	26514778	26514778	+	Frame_Shift_Del
AHDC1	27245	37	1	27875454	27875454	+	Missense_Mutation
COL16A1	1307	37	1	32133218	32133218	+	Silent
CSMD2	114784	37	1	32133218	34383844	+	Silent
LRRC8C	84230	37	1	90179033	90179033	+	Missense_Mutation
SPAG17	200162	37	1	118567972	118567973	+	Frame_Shift_Del
TBX15	6913	37	1	119427935	119427935	+	Missense_Mutation

- **Knock-down sensitivity** in all cell lines for 17.000 genes

	ACH-000004	ACH-000005	ACH-000007	ACH-000009
A1BG	0.1346453616	-0.212445060	0.043317923	0.0705119999
A1CF	0.0755362715	0.233123579	0.066837574	0.0084297636
A2M	-0.1402086015	0.044364933	-0.036196515	0.0271141959
A2ML1	0.0139284337	0.173837240	0.134781001	0.0559267727
A3GALT2	0.0291310328	-0.124389318	0.082995584	0.0463253889
A4GALT	-0.1472838445	-0.298849014	0.119084008	0.0159682666
A4GNT	0.2758291936	0.120259815	0.057116006	0.0535023006
AAAS	-0.3636329615	-0.339925280	-0.352541473	-0.4988600588

- **Annotations** for cell lines (tissue, …)

Project 01: genetic interactions in Cancer cells

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- Select cancer type and corresponding cell lines
- Determine driver mutations from the literature (e.g. EGFR mutations in lung cancer)
- Determine potential synthetic lethal mutations/ copy- number alterations from knock-down screens by splitting **mutated**/**non-mutated** cell lines

non-mutated cell lines

mutated cell lines

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Brief intro to Git(Hub)

Carl Herrmann

Health Data Science Unit - Medizinische Fakultät Heidelberg

Git(Hub)

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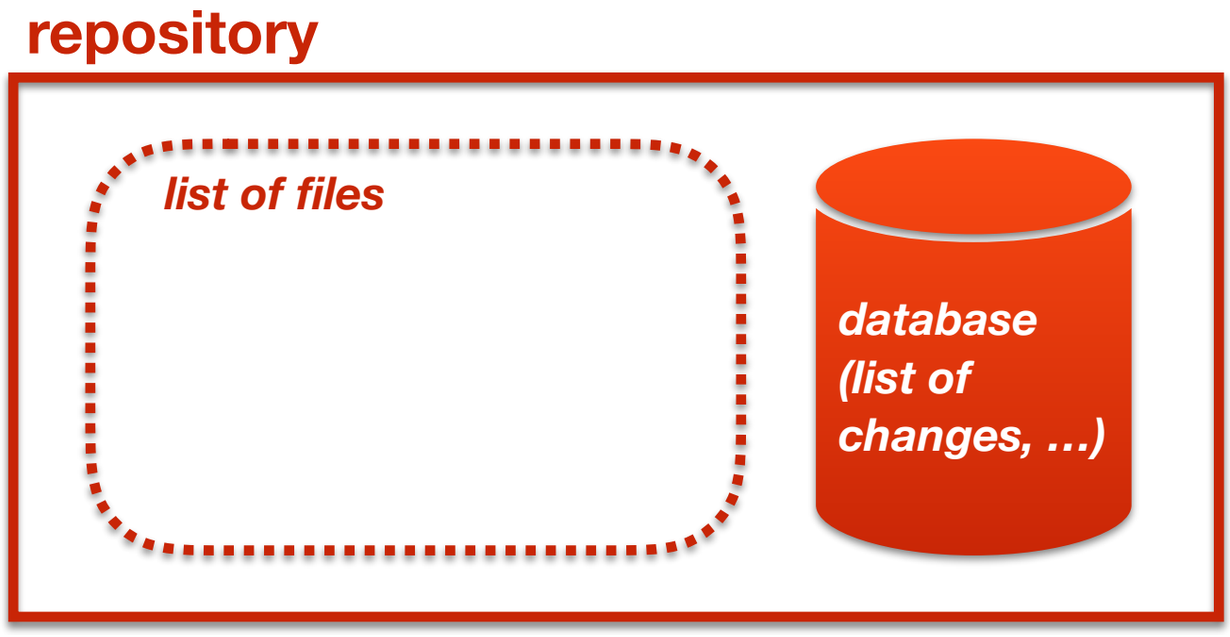
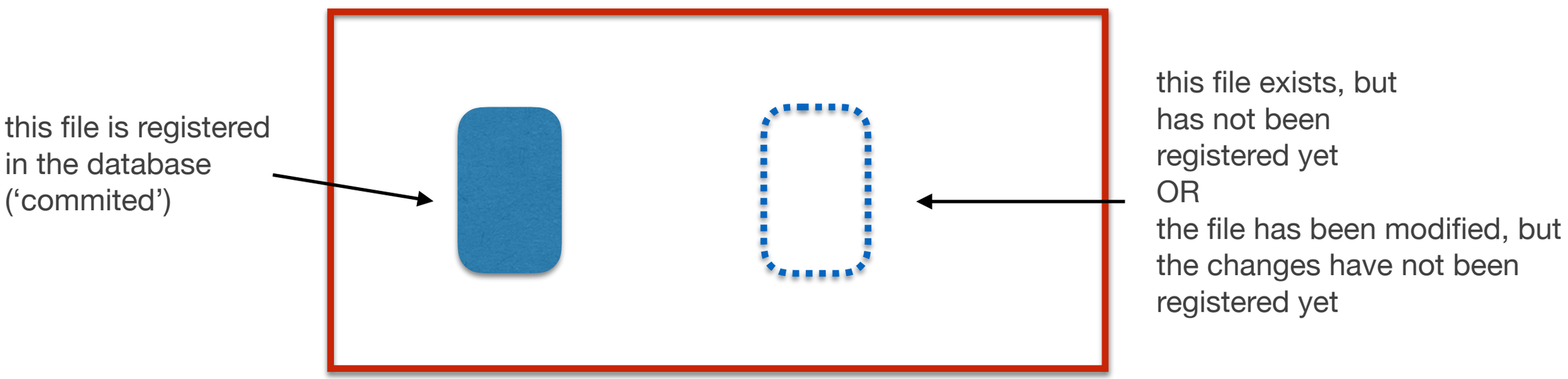
- Git is a **version control system**:
  - allows simultaneous work of different people on the same project
  - tracks the changes (‘**commits**’) made by each member
  - helps solve the **conflicts** between various versions
- GitHub is a plateform which hosts Git projects (‘repositories’)
  - is free to use
  - required to create a (free) account
  - can be used in command line or using GUI tools (‘GitHub Desktop’)

Git repository





1. Cloning an existing repository

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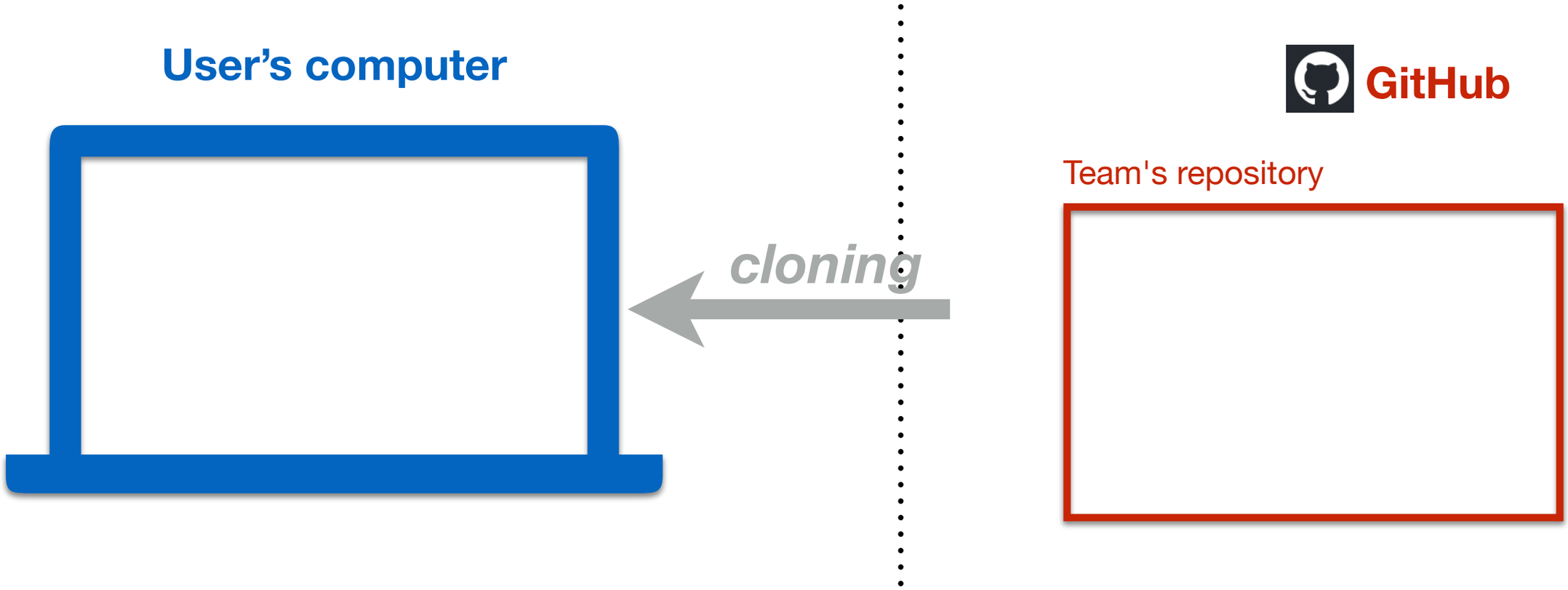
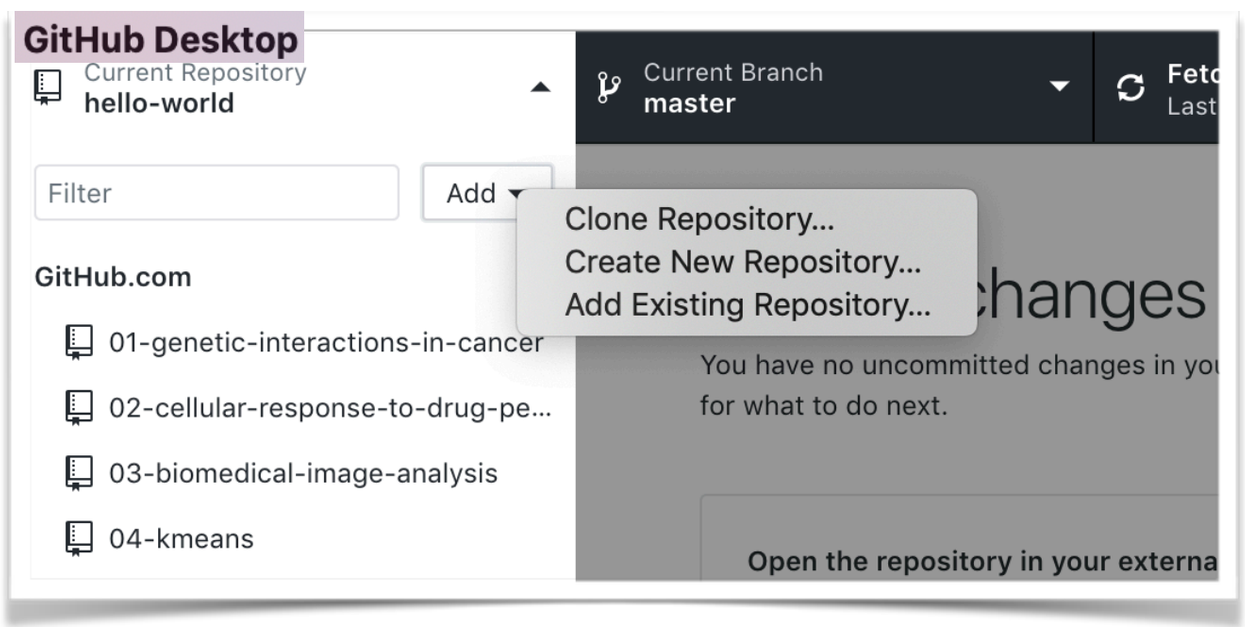
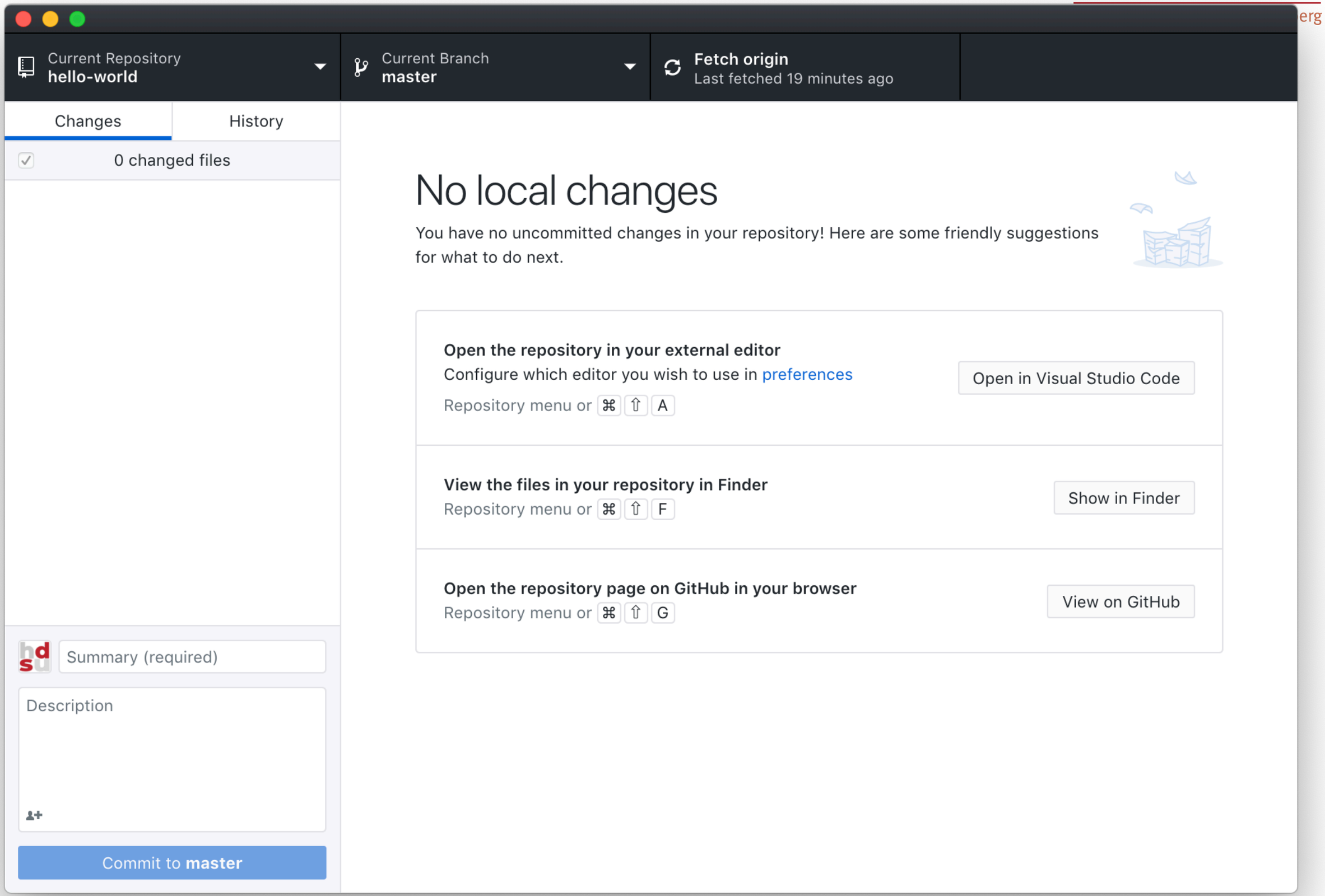
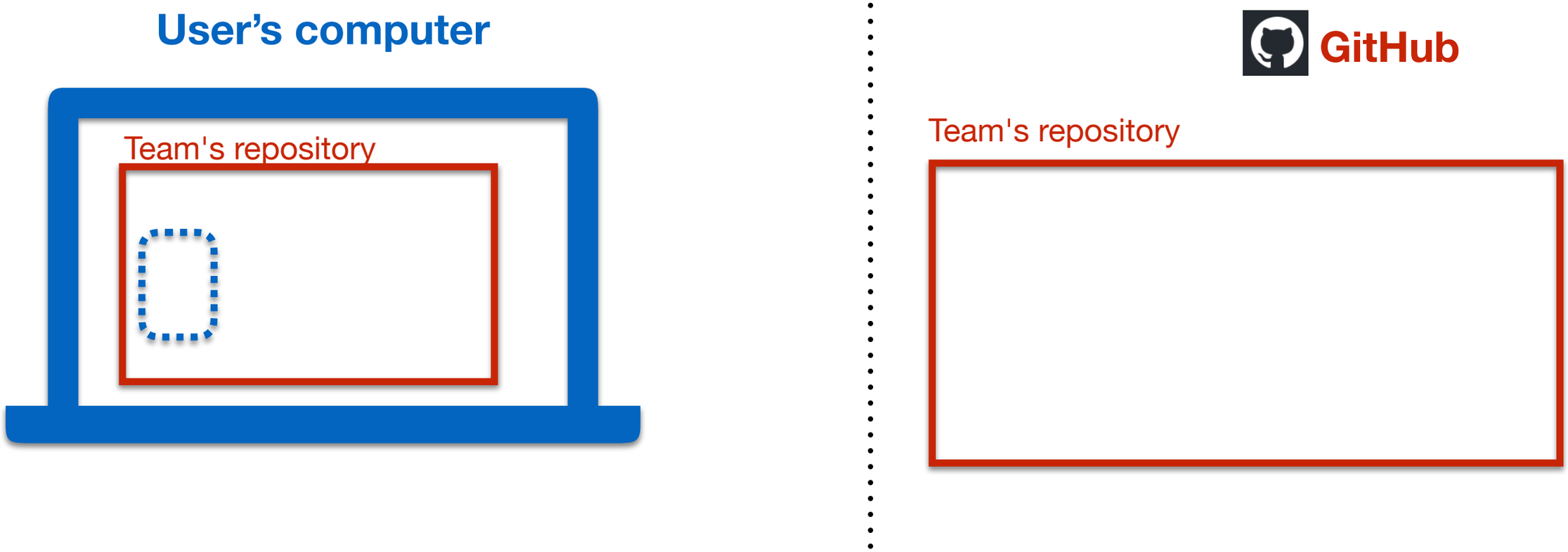


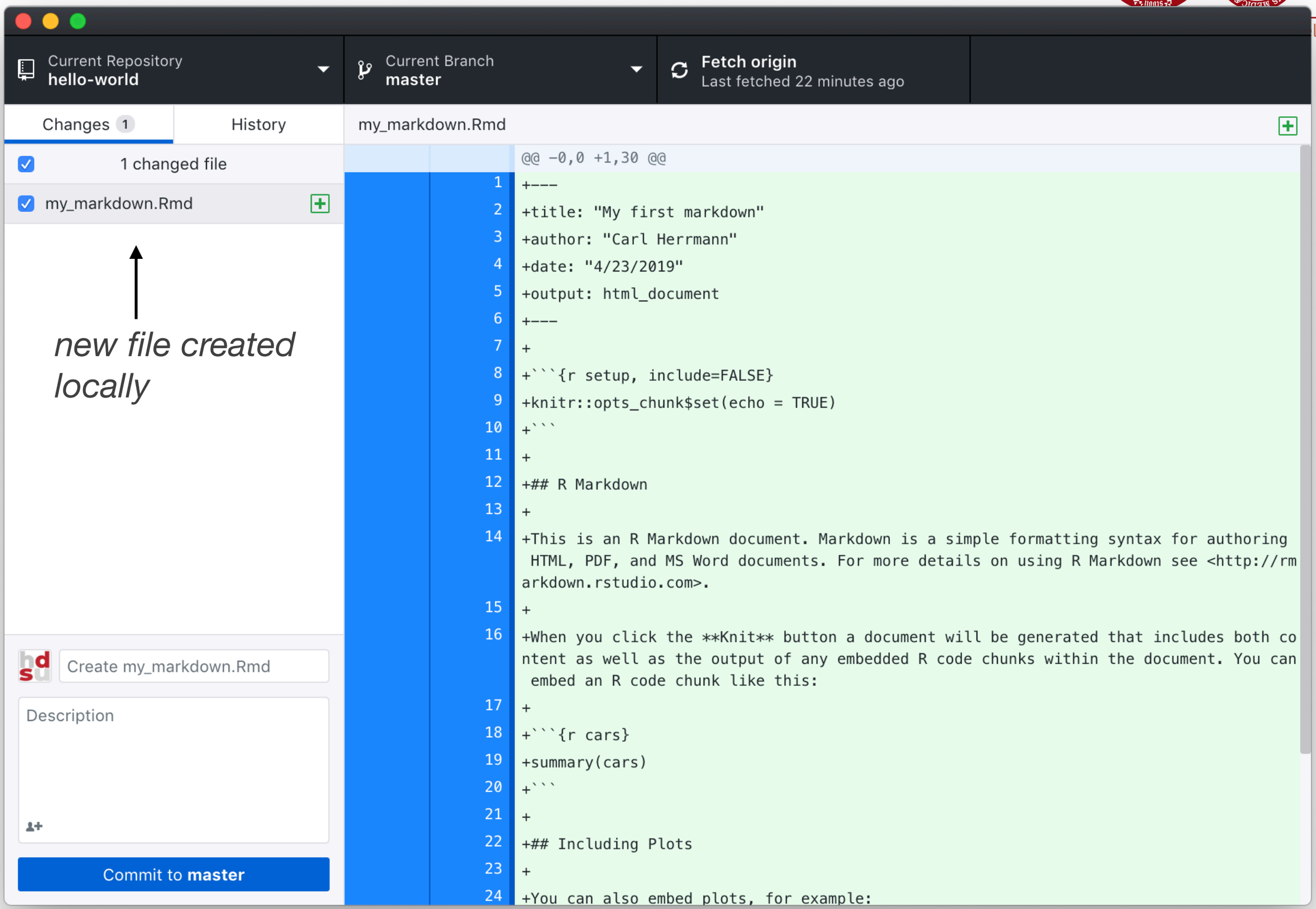



Current Repository
hello-world
Current Branch
master
Fetch origin
Last fetched 19 minutes ago
Changes
History
0 changed files
Summary (required)
Description
Commit to master
No local changes
You have no uncommitted changes in your repository! Here are some friendly suggestions for what to do next.
Open the repository in your external editor
Configure which editor you wish to use in preferences
Repository menu or ⌘ ⇧ A
Open in Visual Studio Code
View the files in your repository in Finder
Repository menu or ⌘ ⇧ F
Show in Finder
Open the repository page on GitHub in your browser
Repository menu or ⌘ ⇧ G
View on GitHub

2. creating a local file



- When a new file is added / modified in the local folder, it is not yet registered in the git database!
- it first needs to be **commited**


Current Repository
hello-world
Current Branch
master
Fetch origin
Last fetched 22 minutes ago
Changes 1
History
my_markdown.Rmd
1 changed file
my_markdown.Rmd
new file created locally
Create my_markdown.Rmd
Description
Commit to master
@@ -0,0 +1,30 @@
+---
+title: "My first markdown"
+author: "Carl Herrmann"
+date: "4/23/2019"
+output: html_document
+---
+
+```{r setup, include=FALSE}
+knitr::opts_chunk$set(echo = TRUE)
+```
+
+## R Markdown
+
+This is an R Markdown document. Markdown is a simple formatting syntax for authoring HTML, PDF, and MS Word documents. For more details on using R Markdown see <http://rmarkdown.rstudio.com>.
+
+When you click the **Knit** button a document will be generated that includes both content as well as the output of any embedded R code chunks within the document. You can embed an R code chunk like this:
+
+```{r cars}
+summary(cars)
+```
+
+## Including Plots
+
+You can also embed plots, for example:

2. Adding a file

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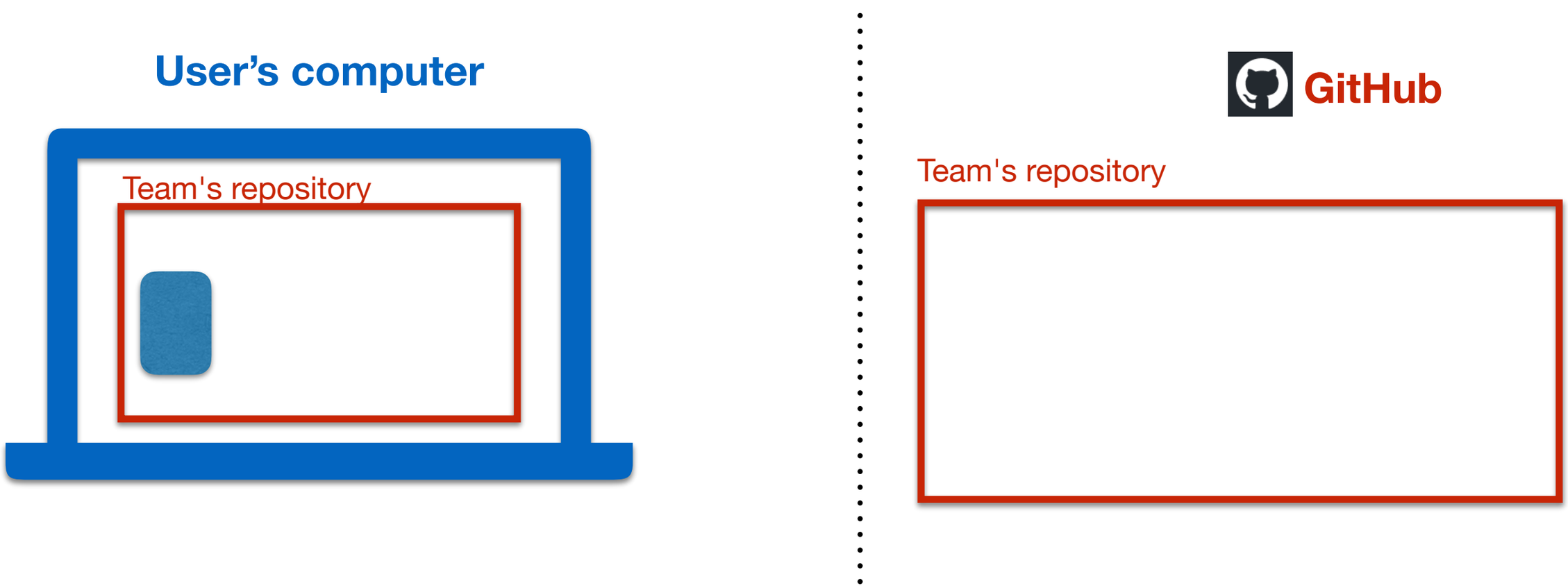

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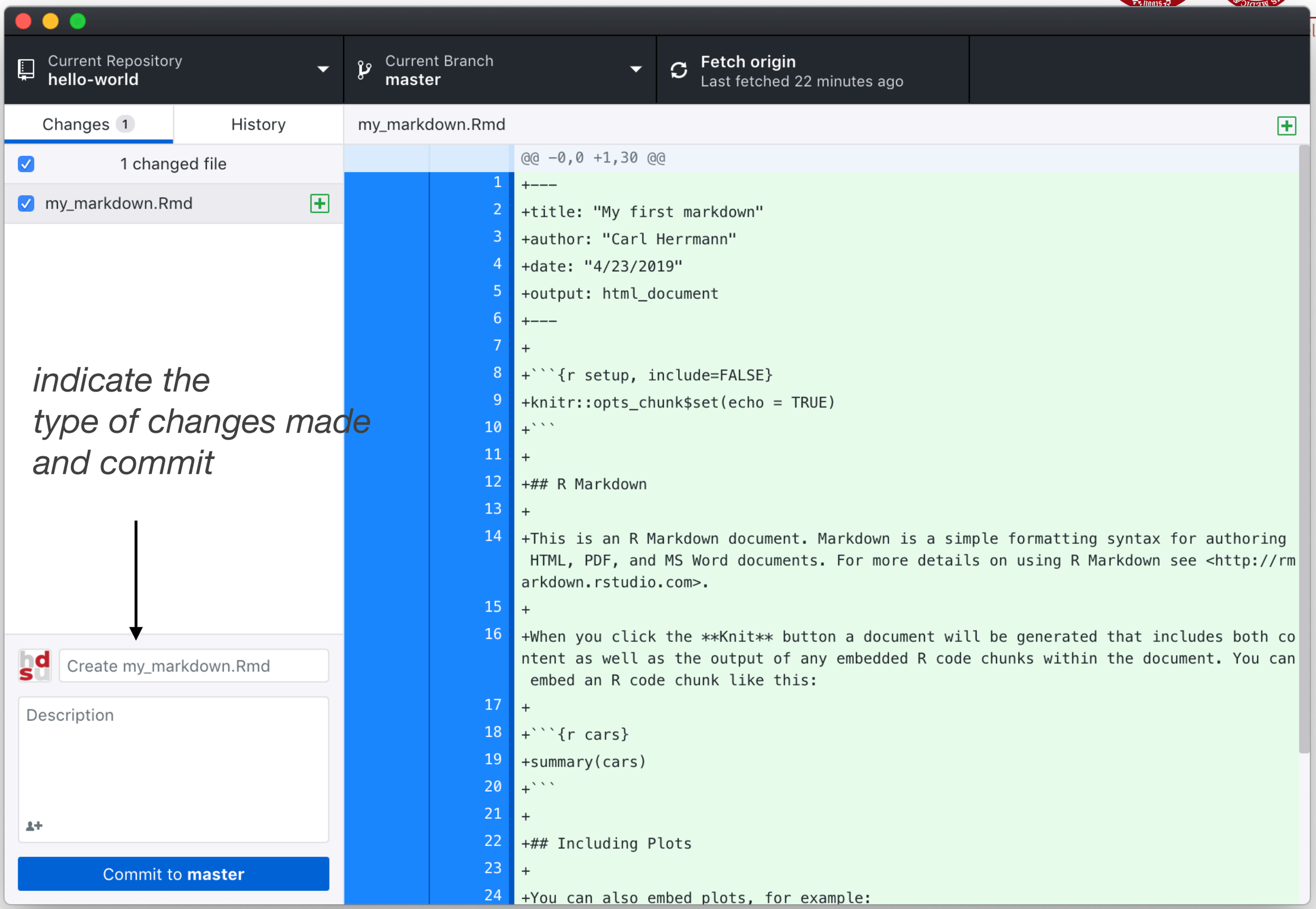
Current Repository
hello-world
Current Branch
master
Fetch origin
Last fetched 22 minutes ago
Changes 1
History
my_markdown.Rmd
1 changed file
my_markdown.Rmd
indicate the
type of changes made
and commit
Create my_markdown.Rmd
Description
Commit to master
@@ -0,0 +1,30 @@
+---
+title: "My first markdown"
+author: "Carl Herrmann"
+date: "4/23/2019"
+output: html_document
+---
+
+```{r setup, include=FALSE}
+knitr::opts_chunk$set(echo = TRUE)
+```
+
+## R Markdown
+
+This is an R Markdown document. Markdown is a simple formatting syntax for authoring HTML, PDF, and MS Word documents. For more details on using R Markdown see <http://rmarkdown.rstudio.com>.
+
+When you click the **Knit** button a document will be generated that includes both content as well as the output of any embedded R code chunks within the document. You can embed an R code chunk like this:
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+```{r cars}
+summary(cars)
+```
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+You can also embed plots, for example:

2. Adding a file

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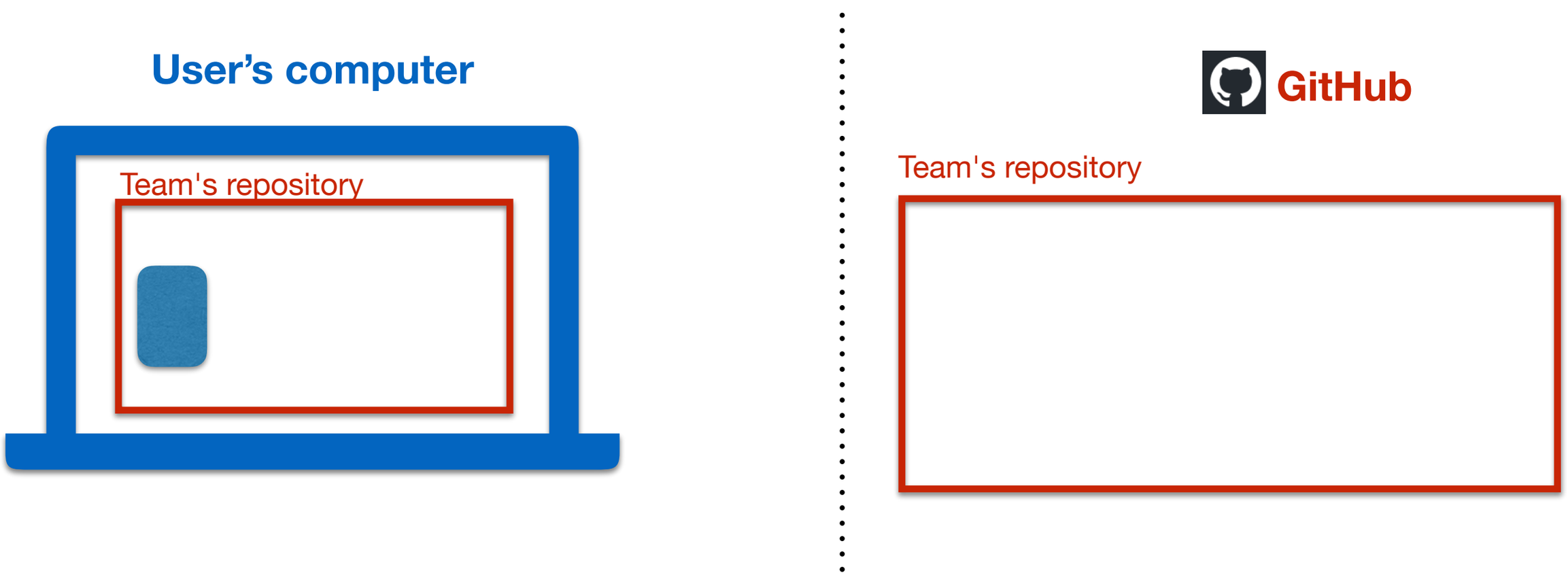

- the file is now commited to the local git repository
- it needs to be pushed to the remote repository on GitHub

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Current Repository
hello-world

Current Branch
master

Push origin
Last fetched 30 minutes ago
1

Changes | History

0 changed files

Summary (required)

Description

Commit to **master**

Committed just now
Create my_markdown.Rmd
Undo

No local changes

You have no uncommitted changes in your repository! Here are some friendly suggestions for what to do next.

Push 1 commit to the origin remote
You have one local commit waiting to be pushed to GitHub
Always available in the toolbar when there are local commits waiting to be pushed or ⌘ P

Push origin

Open the repository in your external editor
Configure which editor you wish to use in preferences
Repository menu or ⌘ ⇧ A

Open in Visual Studio Code

View the files in your repository in Finder
Repository menu or ⌘ ⇧ F

Show in Finder

Open the repository page on GitHub in your browser
Repository menu or ⌘ ⇧ G

View on GitHub

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test repository

Edit

Manage topics

2 commits | 1 branch | 0 releases | 1 contributor

Branch: master | New pull request | Create new file | Upload files | Find File | Clone or download

carlherrmann Create my_markdown.Rmd — Latest commit b2b0bdf 2 minutes ago

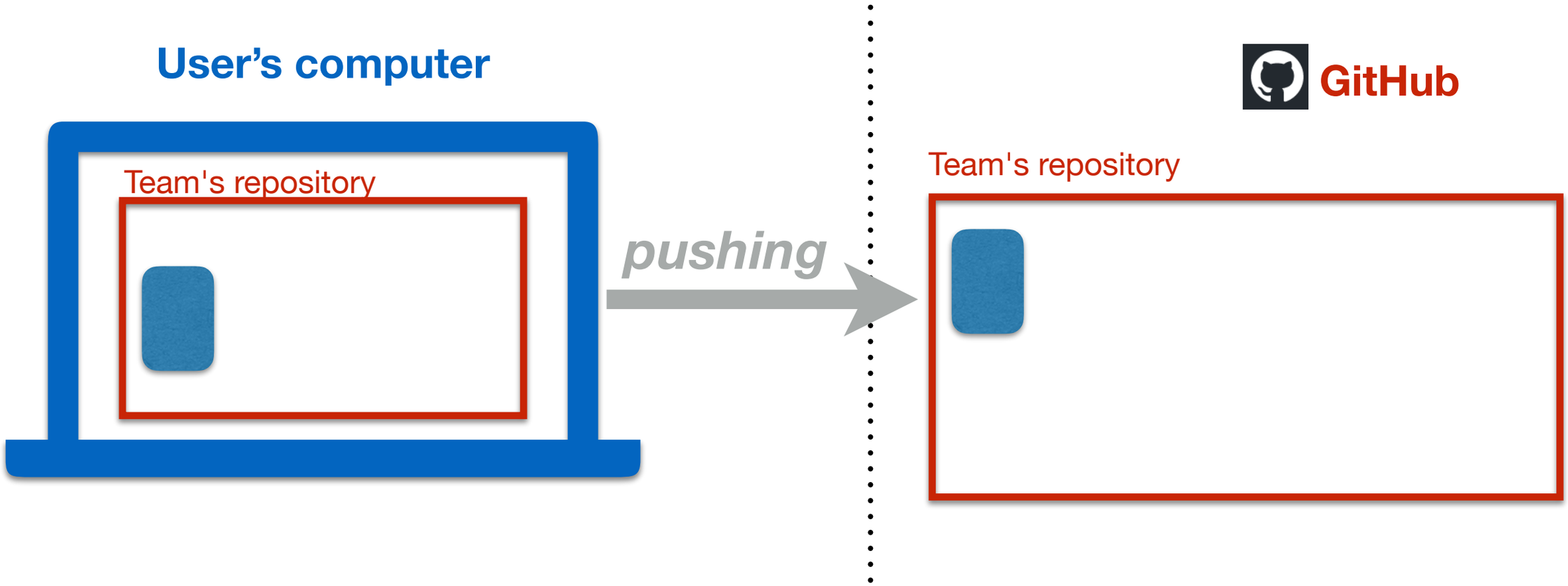
README.md	Initial commit	37 minutes ago
my_markdown.Rmd	Create my_markdown.Rmd	2 minutes ago

README.md

hello-world

test repository

2. Adding a file



- the file is no commited to the local git repository
- it needs to be pushed to the remote repository on GitHub

3. Pulling from the remote repository

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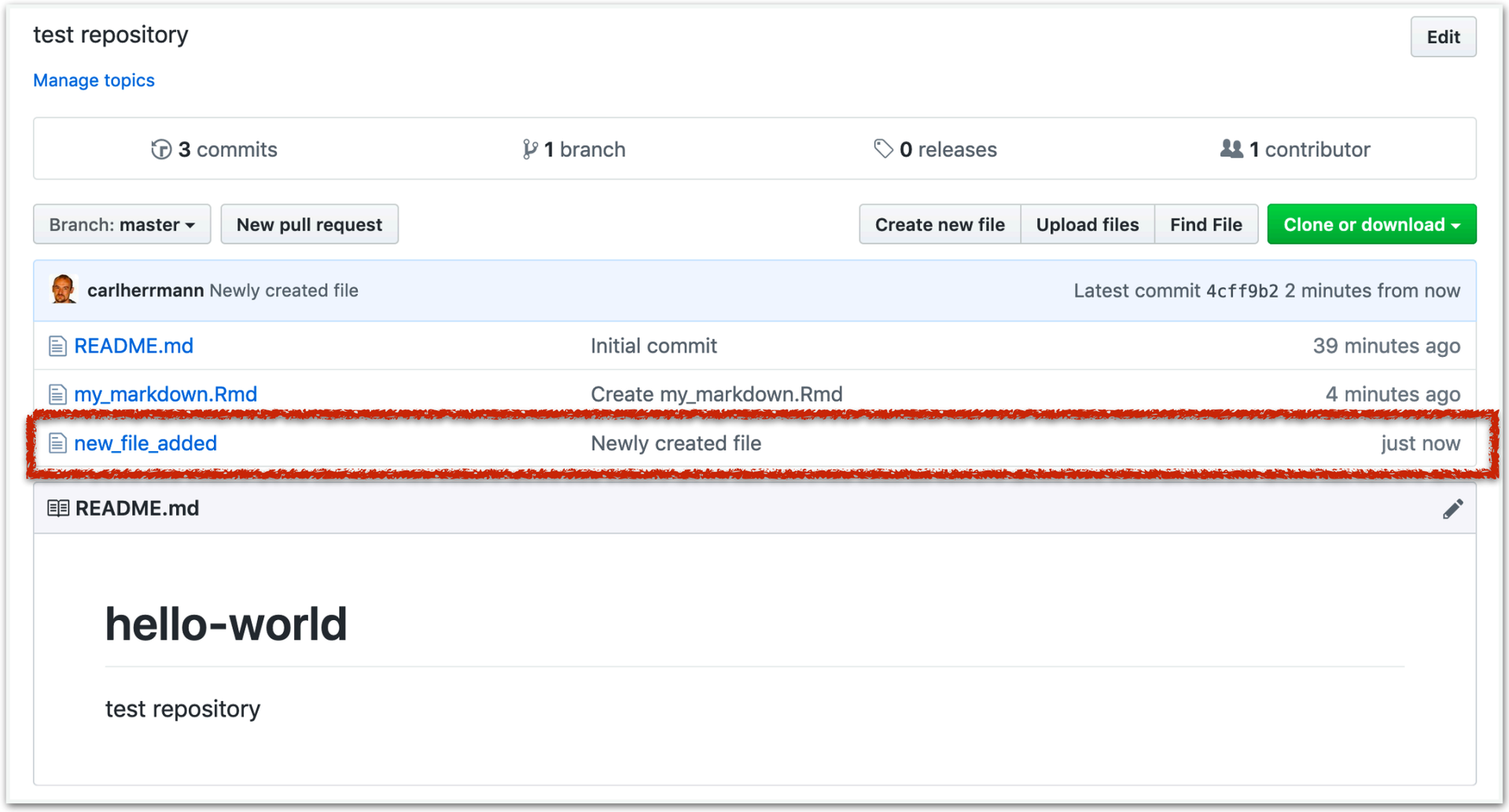
- Someone (probably one of your team mates) has added a new file into the remote repository
- It is not yet in your local repository and need to be **pulled**



3. Pulling from the remote repository

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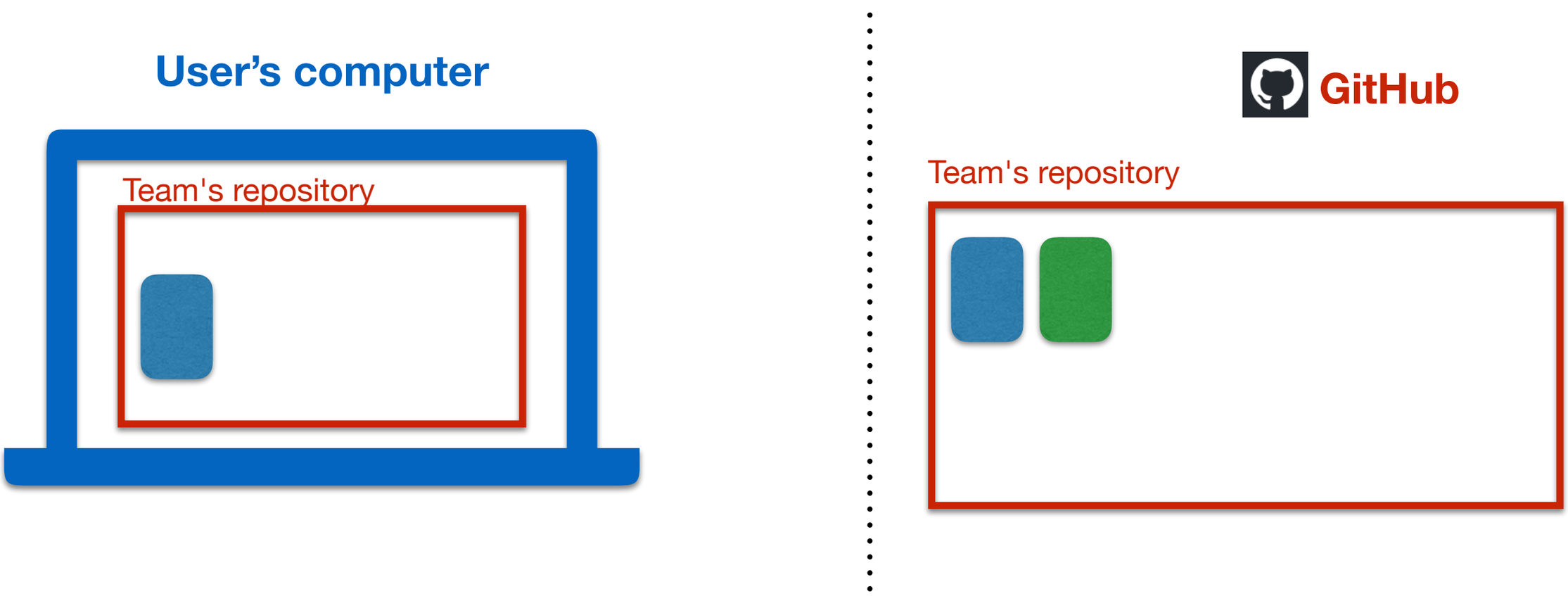
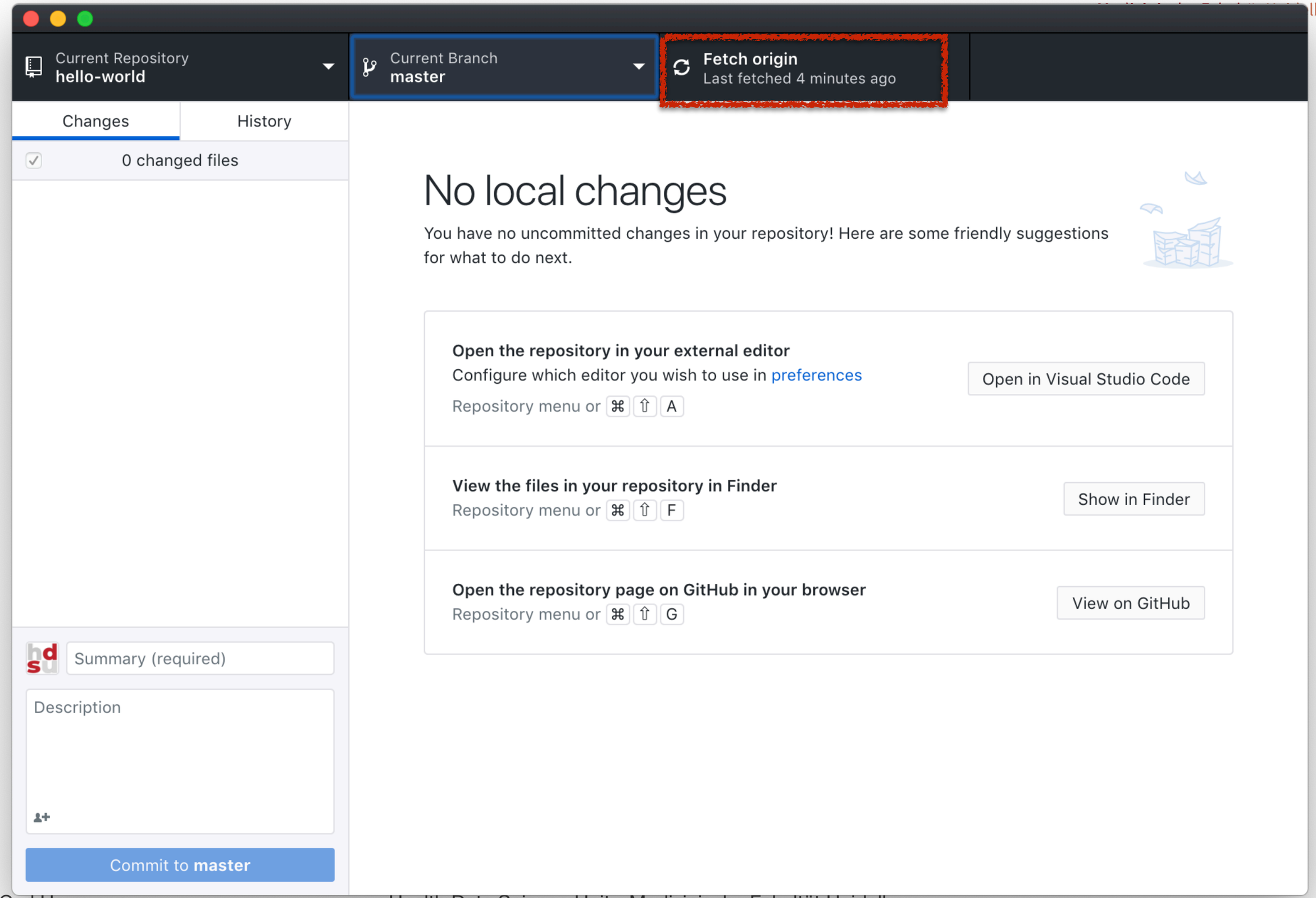
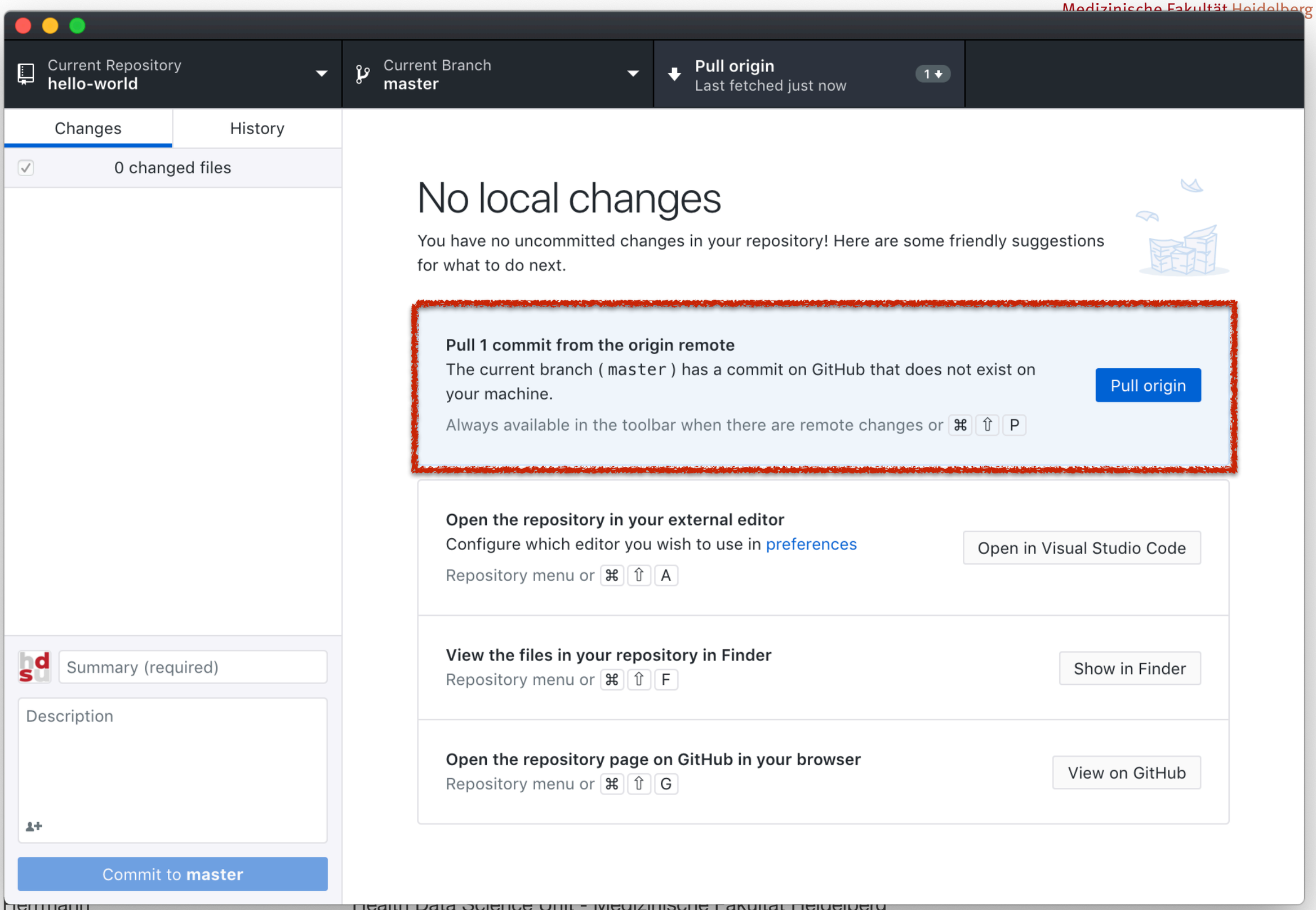
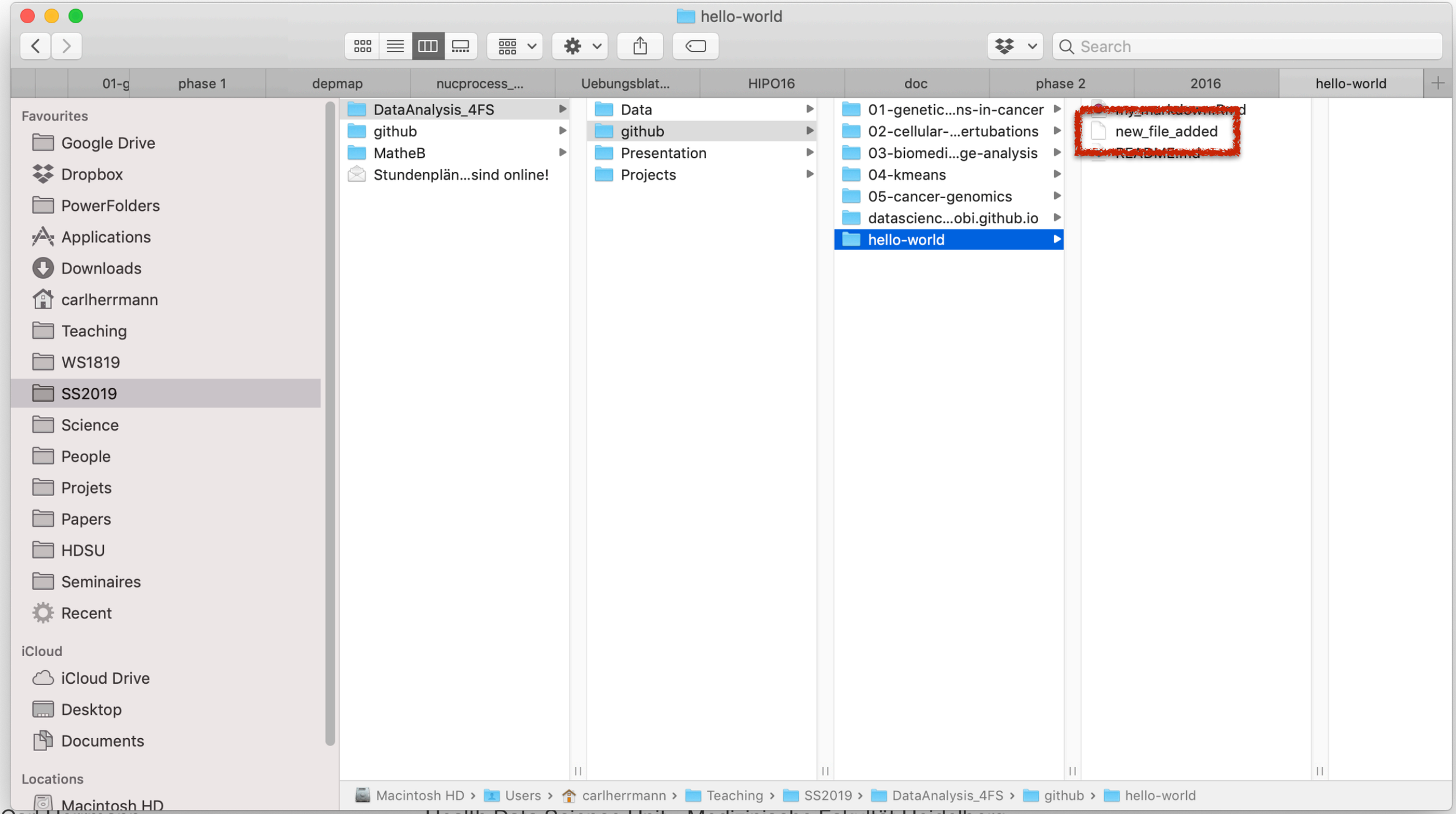



Current Repository
hello-world
Current Branch
master
Fetch origin
Last fetched 4 minutes ago
Changes
History
0 changed files
No local changes
You have no uncommitted changes in your repository! Here are some friendly suggestions for what to do next.
Open the repository in your external editor
Configure which editor you wish to use in preferences
Repository menu or ⌘ ⇧ A
Open in Visual Studio Code
View the files in your repository in Finder
Repository menu or ⌘ ⇧ F
Show in Finder
Open the repository page on GitHub in your browser
Repository menu or ⌘ ⇧ G
View on GitHub
Summary (required)
Description
Commit to master


Current Repository
hello-world
Current Branch
master
Pull origin
Last fetched just now
1
Changes
History
0 changed files
Summary (required)
Description
Commit to master
No local changes
You have no uncommitted changes in your repository! Here are some friendly suggestions for what to do next.
Pull 1 commit from the origin remote
The current branch (master) has a commit on GitHub that does not exist on your machine.
Pull origin
Always available in the toolbar when there are remote changes or ⌘ ⇧ P
Open the repository in your external editor
Configure which editor you wish to use in preferences
Repository menu or ⌘ ⇧ A
Open in Visual Studio Code
View the files in your repository in Finder
Repository menu or ⌘ ⇧ F
Show in Finder
Open the repository page on GitHub in your browser
Repository menu or ⌘ ⇧ G
View on GitHub

- Once the remote repository is pulled, the new file(s) are available locally



3. Pulling from the remote repository

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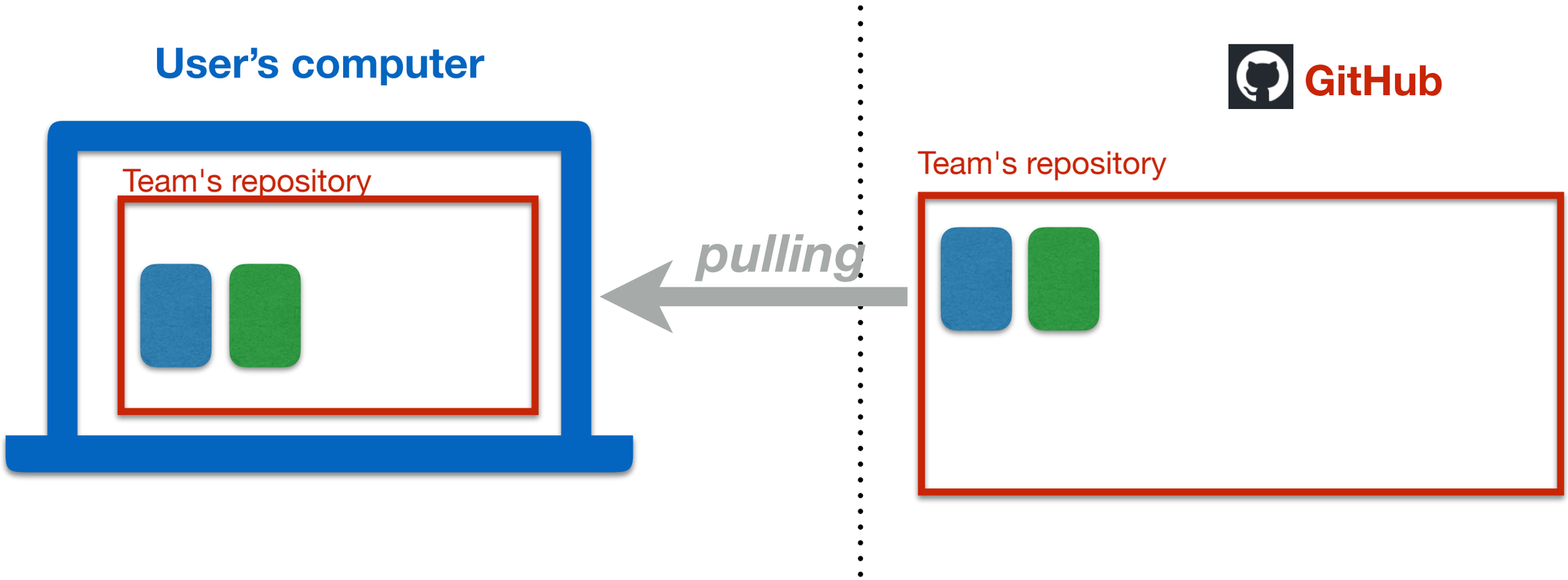

4. conflicting changes

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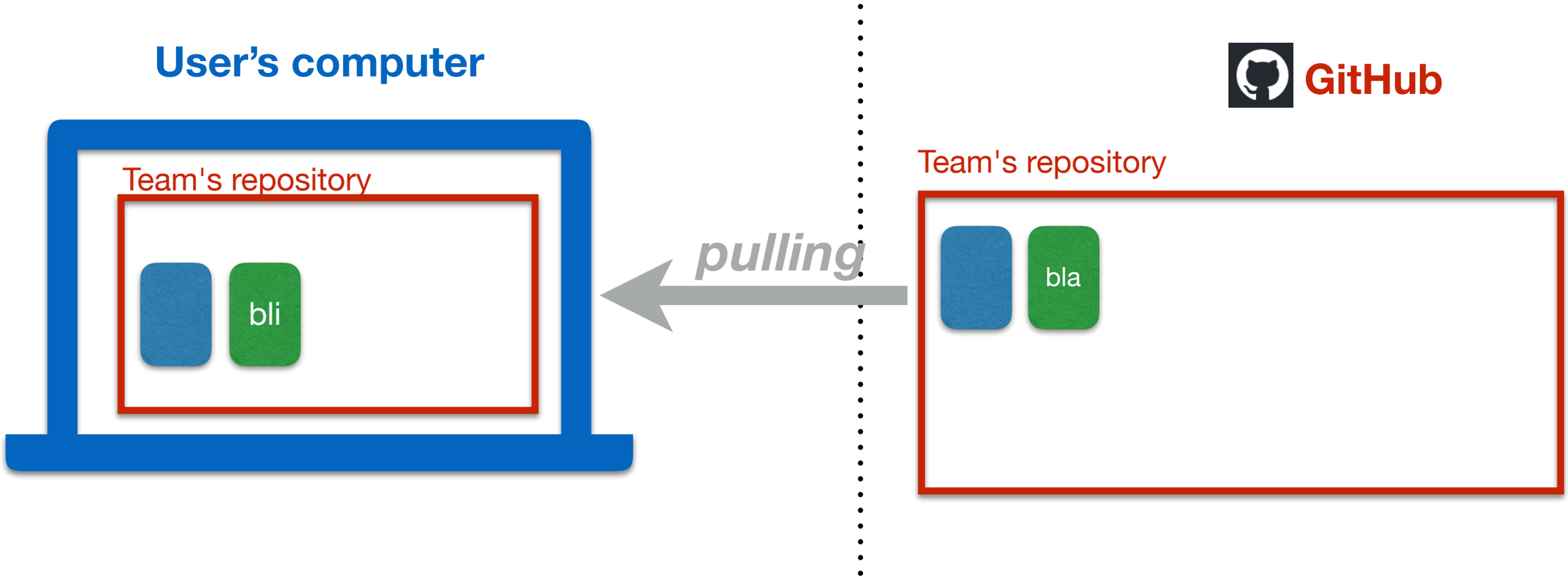
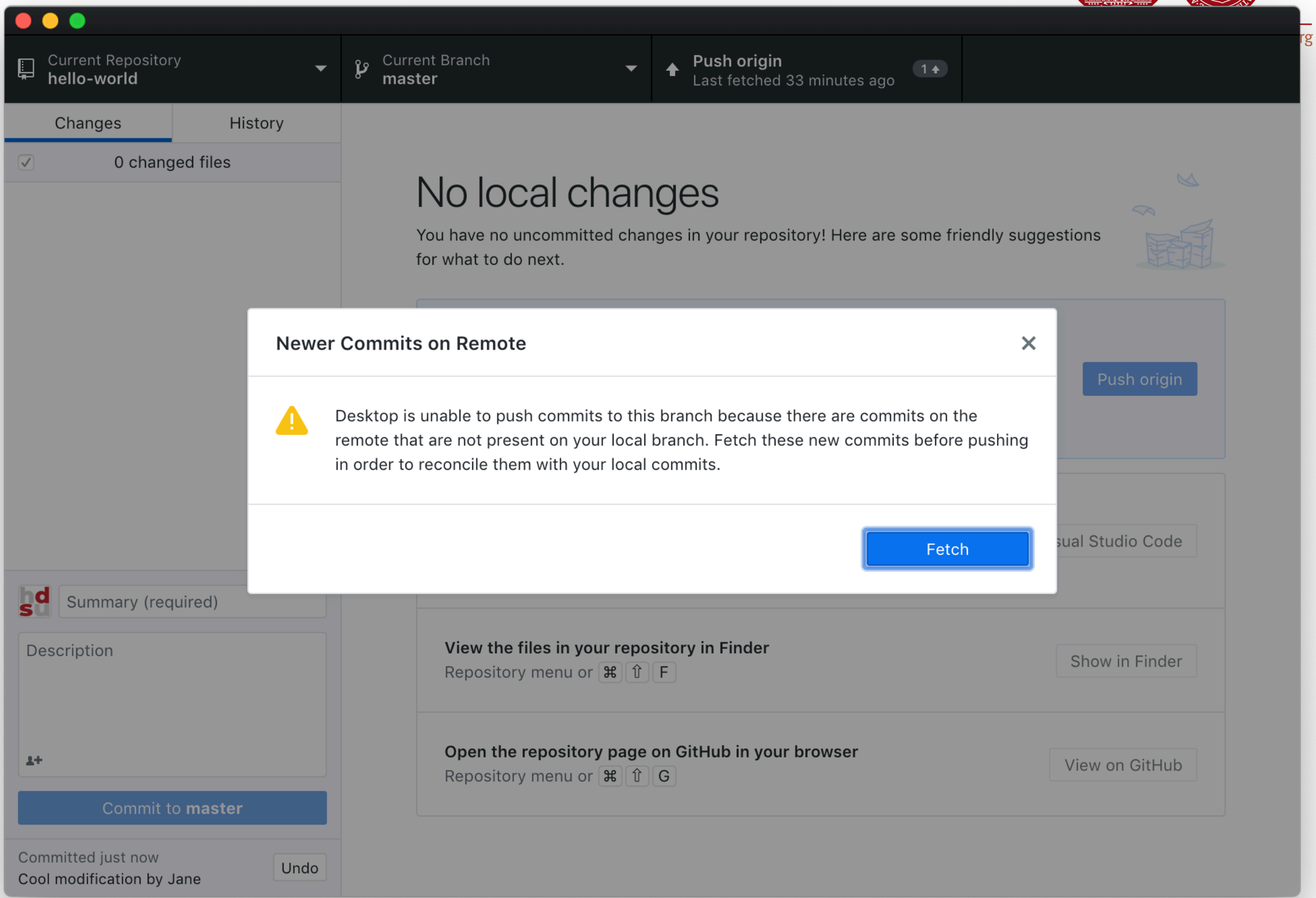
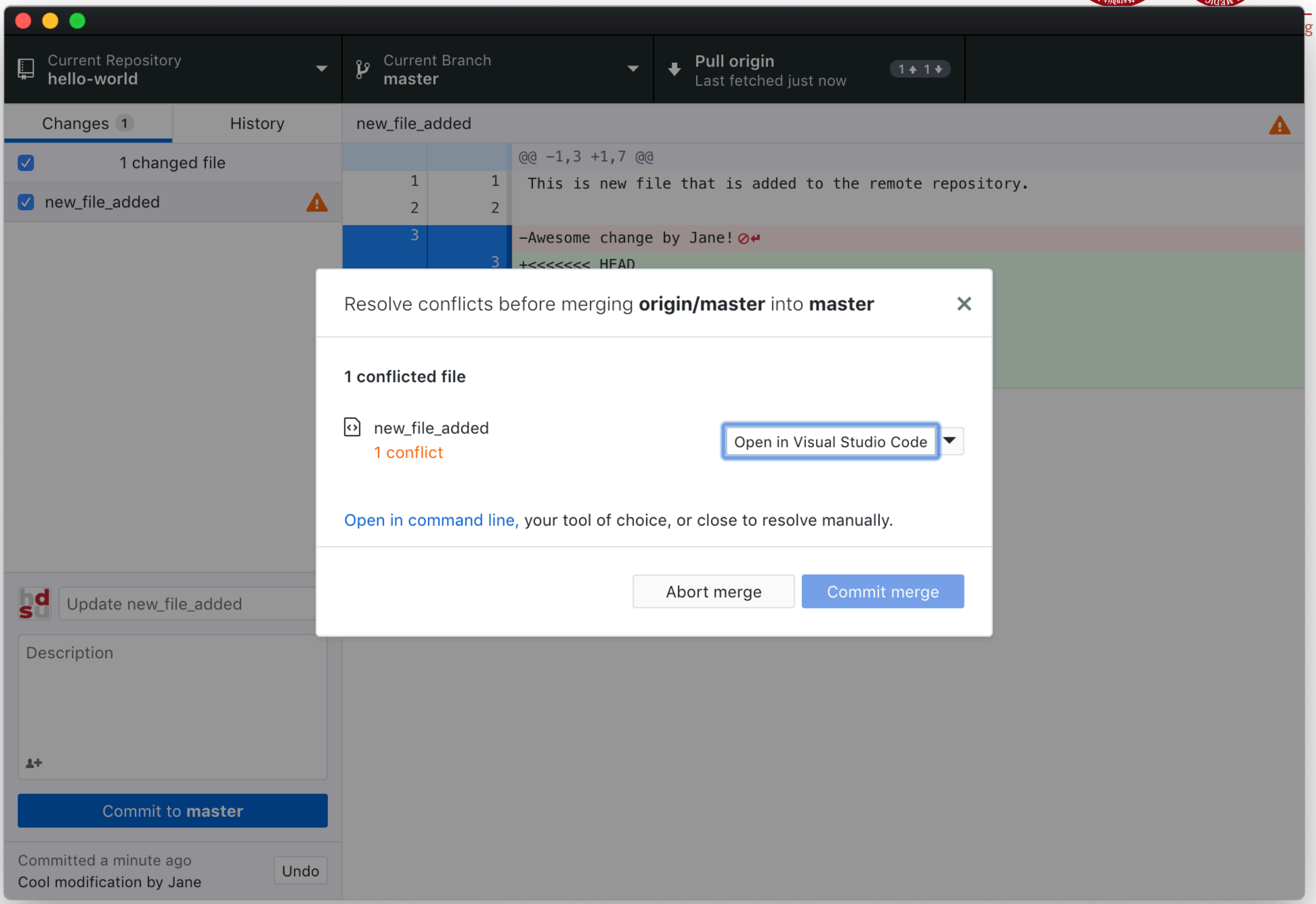



Current Repository
hello-world
Current Branch
master
Push origin
Last fetched 33 minutes ago
1
Changes
History
0 changed files
No local changes
You have no uncommitted changes in your repository! Here are some friendly suggestions for what to do next.
Push origin
Newer Commits on Remote
Desktop is unable to push commits to this branch because there are commits on the remote that are not present on your local branch. Fetch these new commits before pushing in order to reconcile them with your local commits.
Fetch
sual Studio Code
Summary (required)
Description
Commit to master
View the files in your repository in Finder
Repository menu or ⌘ ⇧ F
Show in Finder
Open the repository page on GitHub in your browser
Repository menu or ⌘ ⇧ G
View on GitHub
Committed just now
Cool modification by Jane
Undo


Current Repository
hello-world
Current Branch
master
Pull origin
Last fetched just now
1 ↑ 1 ↓
Changes 1
History
1 changed file
new_file_added
new_file_added
@@ -1,3 +1,7 @@
1 1 This is new file that is added to the remote repository.
2 2
3 -Awesome change by Jane!
3 +<<<<<<< HEAD
Resolve conflicts before merging origin/master into master
1 conflicted file
new_file_added
1 conflict
Open in Visual Studio Code
Open in command line, your tool of choice, or close to resolve manually.
Abort merge
Commit merge
Update new_file_added
Description
Commit to master
Committed a minute ago
Cool modification by Jane
Undo

4. conflicting changes

- Conflicting changes can be resolved with a text editor
- options depend on which editor is used

```
You, a few seconds ago | 2 authors (You and others)
This is new file that is added to the remote repository.

Accept Current Change | Accept Incoming Change | Accept Both Changes | Compare Changes
<<<<<<< HEAD (Current Change)
Awesome change by Jane!
=======
This is a great new modification by Joe!
>>>>>>> af5e9c9981b21a39ed11d09f468bea576d669191 (Incoming Change)
```

local change

changes in the remote file

To do

- Create your own personal GitHub account

- Register your Github user name into the Google Sheet
  - all team members will be added to the corresponding GitHub repo
    - Project 03 - Team 02 → **`project-03-group-02`**

Medizinische Fakultät Heidelberg

(R)markdown

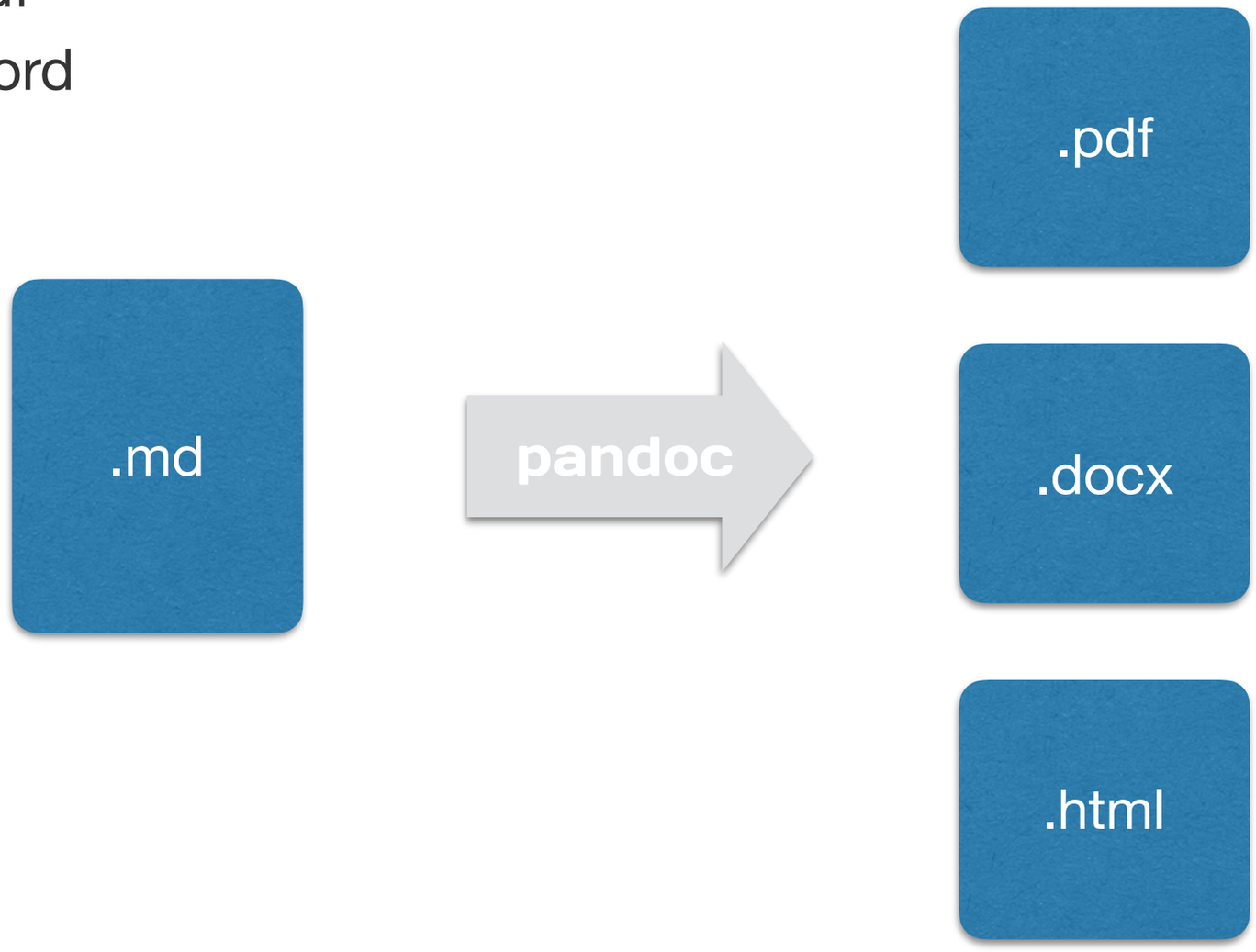
Carl Herrmann

Health Data Science Unit - Medizinische Fakultät Heidelberg

Markdown

Medizinische Fakultät Heidelberg

- Markdown is a way to format plain text with a simple text editor
- Markdown documents can be converted with a **renderer** into
  - html
  - pdf
  - word



Rendering markdown

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markdown

```
# My document

## this is a header

In the text we can *highlight* or put in **bold**.

## making lists

We can make **numbered lists**:

1. first item
2. second item

or unordered lists

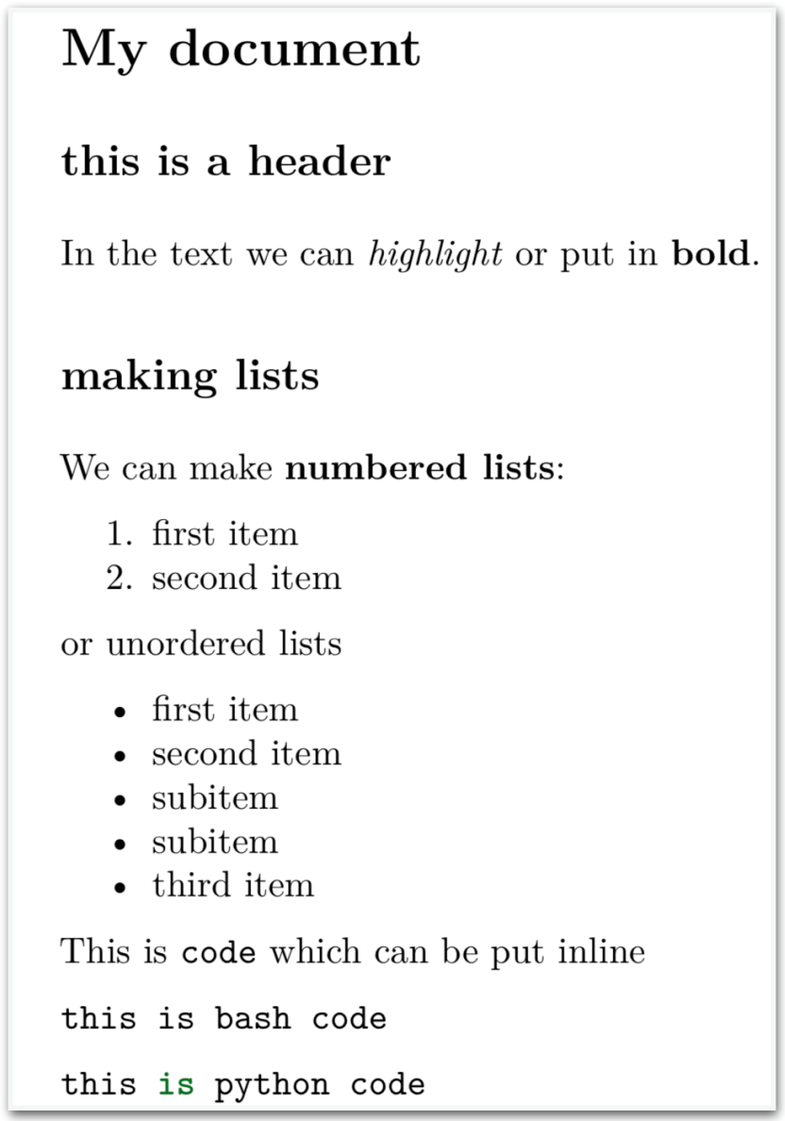
* first item
* second item
  + subitem
  + subitem
* third item

This is `code` which can be put inline

```bash
this is bash code
```

```python
this is python code
```
```

pdf



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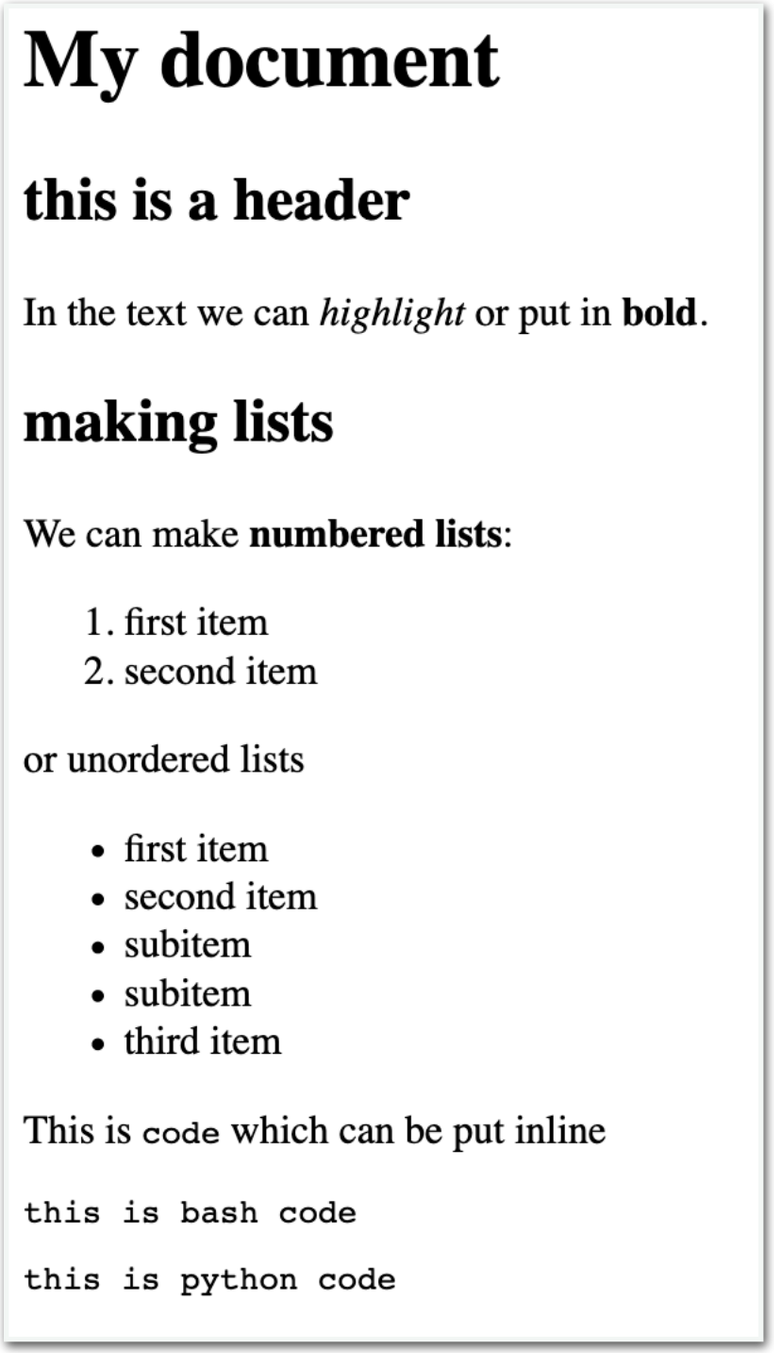
```
this is python code
```

html



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This is `code` which can be put inline

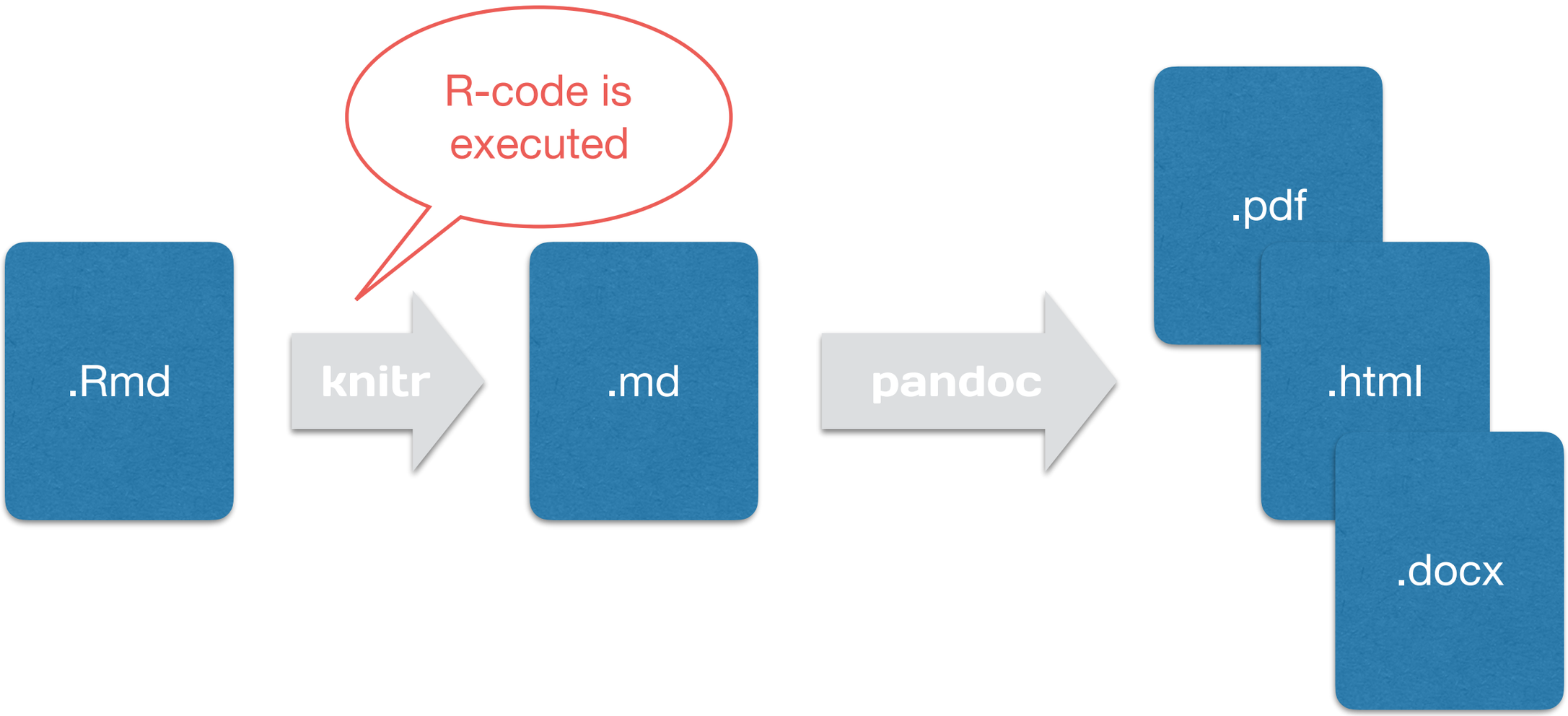
```
this is bash code
```

```
this is python code
```

Rmarkdown

Medizinische Fakultät Heidelberg

- With Rmarkdown, R-code parts can be included into the markdown document
- the R-code will be executed, the result integrated into markdown



Rmarkdown format

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````
---
title: "Project 01"
author: "Carl Herrmann"
date: "4/17/2019"
output:
  html_document:
    keep_md: yes
  pdf_document: default
---
# A Rmarkdown tutorial

This is a brief tutorial on how to use Rmarkdown to create dynamic documents

```{r setup, include=FALSE}
knitr::opts_chunk$set(echo = TRUE)
knitr::opts_knit$set(root.dir='/Users/carlherrmann/Teaching/SS2019/DataAnalysis_4FS')
```

## Load the dataset

```{r read_data}
allDepMapData = readRDS('Data/depmap/DepMap19Q1_allData.RDS')
```

Now plot the distribution of the cell lines according to the tissue type

```{r plot_data}
freq = sort(table(allDepMapData$annotation$Primary.Disease))
par(las=2,mar=c(3,8,3,3));barplot(freq,horiz=TRUE, col='lightgrey')
```
````

header: set options

R code chunks

text in markdown

Rmarkdown chunk options

- Display options can be set for each chunk individually, or for all chunks at the beginning of the document

````
```{r setup, include=FALSE}
knitr::opts_chunk$set(echo = TRUE)
knitr::opts_chunk$set(cache = TRUE)
```
````

valid for all chunks

- echo=TRUE : R-code is displayed in final document
- cache = TRUE : results of all chunks are cached

````
```{r plot_data,fig.height=12,fig.width=12}
freq = sort(table(allDepMapData$annotation$Primary.Disease))
par(las=2,mar=c(3,8,3,3));barplot(freq,horiz=FALSE, col='lightgrey')
```
````

valid for **this** chunks

- set height and width of output figure

Reference

- https://rmarkdown.rstudio.com/
- https://www.rstudio.com/wp-content/uploads/2016/03/rmarkdown-cheatsheet-2.0.pdf
-

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Conda

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(mini)conda

Medizinische Fakultät Heidelberg

- Conda is a tool to easily install software (for example python libraries)
- Conda can be used to create environments, which contain specific software
- These environment are independent of each other, i.e. do not interfere with each other
- Example
  - one environment with Python version 2.7 + libraries
  - one environment with Python 3 + libraries